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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,872	09/29/2005	Tatsuo Hoshino	21407 US C038435/0185010	2413

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EXAMINER	
MEAH, MOHAMMAD Y	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 11/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/528,872	HOSHINO ET AL.	
	Examiner	Art Unit	
	Mohammad Meah	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 6/27/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

With preliminary amendment of this application, the applicant, on date 08/13/2006 elected with traverse group I ((claims 1-7) for examination.

Election/Restriction

During preliminary amendment of this application, the applicant, on date 08/13/2006 elected Group I (claims 1-7) drawn to isolated polynucleotide comprising nucleic acid sequence of SEQ ID NO: 3 and vector for examination. Although applicant did not argue on the merit of election/restriction-office action of date 07/31/2006, since groups II-III (Claims 8-11) comprise host cell and making polypeptide using vector and host cell belong with DNA of group I **Groups I-III (claims 1-11) will be examined** and groups IV-VIII (claims 12-26) of election/restriction-office action of date 07/13/2006 are withdrawn as non-elected groups.

Priority

Acknowledgement is made of applicant's priority date based on application filing date of 09/23/2003 for PCT/EPO3/10573 and foreign application EPO 02021619.8, filed 09/27/02.

Claim Objections

Claim 1(k) is objected in recitation of "undkr." It should be "under." Appropriate correction is required.

Claim 2(m) is objected in recitation of "InISEQ." It should be " in SEQ." or not? Appropriate correction is required.

Claim Rejections

35 U.S.C. 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The claimed invention in claims 8 and 10 are rejected under 35 USC 101 because the claimed invention directed to non-statutory subject matter. Claims 8 and 10 are rejected as non-statutory as the claims recite an organism encompassing transformed humans or the use of human beings , which is non-statutory subject matter. It is suggested that these claims be amended to recite an isolated transformed cell or use thereof.

35 U.S.C 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-2 indefinite in the recitation of "stringent conditions" as the specification does not define what conditions constitute "stringent". While page 10 of the specification describes some conditions, which are intended to be stringent, there is nothing to suggest that other conditions would not also be included within the scope of this term and in the art what is considered stringent varies widely depending on the individual situation as well as the person making the determination. As such it is unclear how homologous to the sequence of a DNA comprising SEQ ID NO: 1, a sequence must be to be included within the scope of these claims.

Claims 1(b) - indefinite in the recitation of " comprising the coding sequence as depicted in SEQ ID NO:2" because it is unclear whether it comprises all of SEQ ID NO:2 or only part of it and if so what part.

Claims 1(a) - indefinite in the recitation of "mature form of SEQ ID NO:3", as the specification does not indicate what portion of SEQ ID NO:3 this corresponds to.

Claim 2 part (t)- "(m) or (a)-" (a) has no antecedent basis.

Claim 4- indefinite in the recitation of "derived from" because it is unclear whether it is obtained from phaffia gene or mutated form of the gene.

Claim 9, the recitation of " baculovirus" make the claim indefinite as baculovirus is not an organism, it is virus.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules with either SEQ ID NO: 2 and any variant of thereof or any DNA which will hybridize to SEQ ID NO: 2 under any conditions or any DNA amplified amplifying Phaffia nucleic acid with primers of SEQ ID NOs: 4-6 or DNA having the limitations of encoding a protein having the sequence of amino acid SEQ ID NO: 3 and any protein variant of thereof having upto 51.3% sequence identity with SEQ ID NO: 3 or any DNA encoding any SQS polypeptide recognized by any antibody against any variant of SEQ ID NO 3 or any fragment thereof. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus, which is insufficient to put one of skill in

the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the DNA of SEQ ID NO: 2 or a DNA encoding polypeptide of SEQ ID NO: 3 having squalene synthase activity, does not reasonably provide enablement for any DNA molecules of SEQ ID NO: 2 or any variant thereof or any DNA which will hybridize to SEQ ID NO: 2 under any stringent condition or any DNA made by amplifying Phaffia nucleic acid with primers of SEQ ID NOs: 4-6 or DNA having the limitations of encoding a protein having the sequence of amino acid SEQ ID NO: 3 and any protein variant of thereof having upto 51.3% sequence identity with SEQ ID NO: 3 or any DNA encoding any SQS polypeptide recognized by any antibody against any variant of SEQ ID NO 3 or any fragment thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, use the invention commensurate in scope with these claims.

Claims 1-11 are so broad as to encompass any DNA molecule comprising any variant of SEQ ID NO: 2 and fragments thereof or any DNA which will hybridize to SEQ ID NO: 2 under any conditions or any DNA made by amplifying amplifying Phaffia nucleic acid with primers of SEQ ID NOs: 4-6 or DNA having the limitations of encoding a protein having the sequence of amino acid SEQ ID NO: 3 and any protein variant thereof having upto 51.3% sequence

identity with SEQ ID NO: 3 or any DNA encoding any SQS polypeptide recognized by any antibody against any variant of SEQ ID NO 3 or any fragment thereof host cells transformed with said DNAs and methods of producing the encoded protein of said DNAs. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number DNAs that encode amino acids sequences of proteins broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide sequence that encodes the amino acid sequence of only one squalene synthase.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any nucleic acid that encode amino acids sequences of proteins broadly encompassed by the claims because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting squalene synthase activity; (B) the general tolerance of squalene synthase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any squalene synthase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including DNA that encode an enormous number of amino acid modifications of the enzyme of SEQ ID NO: 3. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of squalene synthase genes, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 8-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated host cell transformed with the

synthetic nucleic acid, does not reasonably provide enablement for host cells within a multicellular organism that have been transformed with the synthetic nucleic acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 8-9 are so broad as to encompass host cells transformed with specific nucleic acids, including cells in *in vitro* culture as well as cells within any multicellular organism. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of host cells broadly encompassed by the claims. While methods for transforming cells *in vitro* are well known in the art, methods for successfully transforming cells within complex multicellular organisms are not routine and are highly unpredictable. Furthermore, methods for producing a successfully transformed cell within one multicellular organism are unlikely to be applicable to transformation of other types of multicellular organisms as multicellular organisms vary widely. However, in this case the disclosure is limited to only host cells *in vitro*. Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including the use of host cells within a multicellular organism for the production of polypeptide. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, expression of genes in a particular host cell and having the desired

biological characteristics is unpredictable the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is suggested that applicants limit the claims to "An isolated host cell ...".

CLAIM Rejection - 35 U.S.C 102

35 U.S.C 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3, 5-11are rejected under 35 U.S.C. 102(b) as being anticipated by Robinson et al. (Mol & cell boil 1993, pp 2706-2717).

Robinson et al. teaches nucleotide encoding squalene synthase (SQS) of gene from *S. pombe,* vector and transformed cell (*E. coli*) which is 51.3% sequence identity with applicant gene encoding SQS of SEQ ID NO: 3. Robinson et al.polynucleotide encoding *S. pombe* SQS will hybridize with any fragment of applicant nucleic acid encoding SEQ ID NO: 3 under low stringent condition.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Examiner, Art Unit 1652

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